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EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,249	KURODA ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/1/09 & 2/21/10*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-7,9,14,15,22,24 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-7,9,14,15,22,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/1/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *attachment*.

DETAILED ACTION

1. This Office action is in response to the amendment filed September 1, 2009, and January 21, 2010. Claims 2, 48, 10-13, 16-21, 23 and 26-28 have been cancelled. Claims 1, 3, 5-7, 9, 14, 15, 22, 24 and 25 are pending and are examined in this Office action.

Information Disclosure Statement

2. Applicant's IDS, filed on September 1, 2009, is acknowledged and considered, except for JP 08-504088 because the Abstract is not in English.

Specification

3. (**Prior objection-withdrawn**) The sequence listing and CRF, which contain SEQ ID NOs: 1-29 as originally filed, submitted on January 5, 2010, is acknowledged. The objection to the specification, for introducing new sequences SEQ ID NOs: 30 to 244 into the application on December 16, 2008, is therefore withdrawn.

Claim Objections

4. (**New objection**) Claims 1, 3, 5, 6, 22, 24 and 25 are objected to because of the following informalities: "L-protein" in Claim 1 should be spelt out when it appears for the first time. No "-" is needed in word of "surface antigen large (L) protein".

5. Claims 3/22, 5/24 and 6/25 are duplicate thereof. Appropriate correction is required.

6. Claim 3 is suggested to be amended as "...wherein the antibody is displayed on ~~a~~ the surface of the nanoparticles ~~surface~~ by binding to a ZZ tag..."

Claim Rejections - 35 USC § 112, second paragraph

7. The following is a quotation of the second paragraph of 35 USC 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. (**Prior rejection-withdrawn**) The rejection of Claim 9 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention, is withdrawn in view of amendment to the claim. The rejection of Claims 2 and 8 is moot in view of the cancellation of the claims.

9. (**New rejection-necessitated by the amendment**) Claims 1, 3, 5-7, 9, 14, 15, 22, 24 and 25 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Claim 1 is indefinite because the limitation "cancer specific antibody" is not explicitly defined in either the claims or the specification. One of ordinary skill in the art cannot be reasonably apprised of the metes and bounds of the invention without a clear definition of "cancer specific antibody".

In response to Applicant's argument:

10. Applicant argues that the term "cancer specific antibody" well known to those skilled in the art. The definition of the term "cancer specific antibody" can be explicitly

found on page 16, lines 18-20 of the specification, e.g., "a cancer specific antibody that recognizes a surface molecule of a specific cancer cell as an antigen".

11. However, this argument is not convincing. The full context of paragraph 2, including lines 18-20 of the specification, is recited below:

> The type of antibody bound to the particle surface **is not particularly limited** as long as it recognizes a surface molecule of a specific cell as an antigen. **For example**, the antibody **may be** a cancer specific antibody that recognizes a surface molecule of a specific cancer cell as an antigen. **As another example**, an antibody may be used that specifically recognizes an antigen on the surface of a specific cell as a growth factor receptor or cytokine receptor. Other than these examples, various types of antibodies specific to other types of antigens displayed on the cell surface or tissue surface may be used as well (Emphasis added).

First, this citation above from the specification is not limiting definition for the term of "cancer specific antibody" in the patent application, but one of embodiments. The specification does not explicitly teach what molecules are "cancer -specific". Since most cancer-specific molecules (cancer makers) are not well known in the art, one of ordinary skill in the art cannot be reasonably apprised of the metes and bounds of the invention without a clear definition of "cancer specific antibody". This rejection affects all dependent claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

12. The following is a quotation of the first paragraph of 35 USC 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. (**Prior rejection-maintained**) The rejection of Claims 1-3, 5-9, 14-16, 22, 24 and

25 under 35 USC 112, first paragraph, as failing to comply with the enablement requirement, **is maintained** for the reasons restated below:

14. Claims 1-3, 5-9, 14-16, 22, 24 and 25 as amended are directed to a substance carrier comprising nanoparticles of a modified HBV surface large antigen, the hollow nanoparticles displaying an antibody against a specific cell or specific tissue, and encapsulating a substance to be transferred into a cell for treating a disease, wherein the antibody is a cancer specific antibody or anti-virus protein antibody.

15. Although the claims have been amended from prior "drug" to "a substance carrier", the specification indicates that the term "a substance carrier" is equivalent to "a drug" in this application; see e.g. Para 3, p. 16; and Para 2, p. 17. Therefore, according to the specification, the term "a substance carrier" still reads on "a drug". The rejection is maintained for the reason set for in Para 12 and 13 of the previous Office action.

In response to Mr. Kuroda's Declaration under 37 CFR 1.132 filed on September 1, 2009.

16. The Office acknowledges the Declaration of Mr. Kuroda under 37 CFR 1.132 filed on September 1, 2009. However, Mr. Kuroda's Declaration is not sufficient to overcome the rejection because the evidence submitted by Mr. Kuroda is not commensurate with the scope of the claimed invention for the following reasons:

17. According to MPEP 2164.05, to review a declaration, "the examiner should carefully compare the steps, materials, and conditions used in the experiments of the declaration with those disclosed in the application to make sure that they are commensurate in scope; i.e., that the experiments used the guidance in the specification as filed and what was well known to one of skill in the art. Such a showing also must be

commensurate with the scope of the claimed invention, i.e., must bear a reasonable correlation to the scope of the claimed invention". In the present case, Mr. Kuroda specifically presented three drugs in three experiments in his Declaration: Experiment 1 shows an HBsAg L protein particle comprising a low-molecule weight compound calcein. However, this particle is not claimed subject matter because calcein is known to be a fluorescent dye, not "a substance to be transferred into cell for treating a disease". The particle does not display any "cancer specific antibody or anti-virus protein antibody" as required by the claims. Experiment 2 shows an HBsAg L protein particle comprising DXR. However, this particle does not display any "cancer specific antibody or anti-virus protein antibody" as required by the claims. Experiment 3 shows a BNC (HBsAg-ZZ)-liposome complex containing fluorescent beads. However, this complex does not encapsulate any substance in the HBsAg L protein particle. Rather, the fluorescent beads are apparently conjugated outside of HBsAg L protein particle; Also see discussion Para 22-25 below. The HBsAg particle does not display "a cancer specific antibody or anti-virus protein antibody", either. Moreover, none of the three particles presented in the Declaration have been shown to be efficacious for treating any specific diseases as cited by the claims. Thus, none of nanoparticles presented in the Declaration have complete structural and functional properties of the claimed "substance carrier" (drug). It is noted that Applicants particularly argue these key structural and functional properties cited in the claims; see e.g., Para 3, p. 10; Para 2, p. 11; and Para 1, p. 12, Remarks filed on September 1, 2009. Thus, based on the limitations set in the claims and the same standard as Applicant set in the Remarks, the particles presented by Mr. Kuroda do not support the claimed subject matter.

In response to Applicant's argument:

18. Applicants assert (1) that Applicants have amended the claims to recite "substance carrier". The main purpose of the "substance carrier" is to carry the substrate to a target cite (for example, cells and tissues.

19. This argument is not convincing for the reason set forth in Para 15 above.

20. Applicants argue (2) that the specification describes use of an HBsAg particle in the experimental system for the treatment of carcinoma of nude rats, which is a model of the treatment of human diseases. The nude rat can be used as the model of the treatment of human diseases, which is well known by those skilled in the art.

21. This argument is considered but found not persuasive. The scope of the claims encompasses a drug comprising HBsAg L protein and a substance, which can treat any disease, not only carcinoma. One of ordinary skill in the art does not recognize nude rats are a model for the treatment of any human diseases. As indicated in Para 13 of the previous Office action, the art indicates that it is not certain that the claimed drug comprising HBsAg L protein and undefined substance can treat any disease. Therefore, Applicant's argument is not convincing.

22. Applicants further argue (3) that **the encapsulating method** usable in the present set of claims may select a variety of methods and is not limited to a specific method, for example, an electroporation method, ultrasonic method, simple diffusion method, and a method using charged lipids (see e.g. line 30, page 17 to line 3, page 18 of the English Specification). With these methods, adjusting a ratio at which the substance to be transferred into a cell is encapsulated into a particle may be possible. Applicants submit that these methods are well-known by one skilled in the art, and further, one skilled in the art would understand from the specification that encapsulating various substances to be transferred into a cell into the hollow nanoparticles is possible.

23. This argument is not convincing because, first, this argument is not supported by the specification. The teaching of specification is recited below:

"These target-cell substances **may be incorporated into** the hollow nanoparticles by various methods commonly used in chemical or molecular biological experimental techniques. Some of the preferred examples include an electroporation method, ultrasonic method, simple diffusion method, and a method using charged lipids" (Recited from bridge Para between p.17 and 18, including line 30, page 17 to line 3, page 18).

In view of the whole context of the paragraph, the specification teaches methods of "incorporating", not "encapsulating" a substance, "include an electroporation method, ultrasonic method, simple diffusion method, and a method using charged lipids". Unlike "incorporating", the term "encapsulate" means "to enclose in" (see attached citation from Merriam Webster Dictionary). For example, one of ordinary skill in the art also understand that "encapsulating" a dug in a capsule mean to enclose the drug in the capsule, not on the capsule or outside of the capsule.

24. The claims require the hollow nanoparticles of HBsAg L protein "encapsulating a substance to be transferred into a cell for treating a disease", which means **enclosing** a substance **in** the particle (emphasis added). The instant specification also teaches that "a substance to be transferred into a cell for treating a disease...**is encapsulated in** hollow nanoparticles of a particle-forming protein (for example, hepatitis B virus surface-antigen protein"; see e.g. Abstract; Para [0016][0021][0025], etc. of US publication of the specification.

25. However, not all methods of incorporating a substance into a nanoparticle, as listed in the specification; see citation above, is capable of encapsulating the substance inside the particle. For example, the Experiment 3 of the Declaration shows that "the

method of using charged lipids" does not result in encapsulating fluorescent beads inside the HBsAg L protein particle, but outside of the particle. Thus, Applicants' argument regarding "encapsulating method" in the specification is not supported by either the specification or the Declaration. Rather, both the specification and the Declaration show that the specification lacks teaching and guidance how to encapsulate any undefined substances in HBSAg L protein particles.

26. For the reasons discussed above and reasons set forth in Para 15 of the previous Office action, Applicant's argument and Mr. Kuroda's Declaration is not sufficient to overcome the rejection under 112, 1st paragraph.

Claim Rejections - 35 USC § 102

27. The following is a quotation of the appropriate paragraphs of 35 USC 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

28. (**Prior rejection-withdrawn**) The rejection of Claims 1, 5-7, 14, 16, 24 and 25 under 35 USC 102(b) as being anticipated by O'Riordan (WO 99/40214, International publication date: August 12, 1999), **is withdrawn** in view of the amendment to the claims. Claim 1 has been amended as the particle-forming protein including a modified HBsAg large protein. The rejection is therefore withdrawn.

29. (**Prior rejection-withdrawn**) The rejection of Claims 1, 5-7, 14, 16, 24 and 25 under 35 USC 102(b) as being anticipated by Kuroda (WO 01/64930, which is

PCT/JP01/00926, International publication date: September 7, 2001, cited in IDS. The US2003/0092069, which is the National stage of PCT/JP01/00926, is cited as the English translation of WO 01/64930), **is withdrawn** in view of the amendment to the claims.

Claim Rejections - 35 USC § 103

30. The following is a quotation of 35 USC 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 USC 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of their obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 USC 103(c) and potential 35 USC 102(e), (f) or (g) prior art under 35 USC 103(a).

31. (**Prior rejection-withdrawn**) The rejection of Claim 15 under 35 USC 103(a) as being unpatentable over O'Riordan (WO 99/40214, as applied to Claims 1, 2, 5-7, 14, 16, 24 and 25 above, and further in view of Rosenfeld (1997; Annals of Surgery 1997; 225(5):609-618), is withdrawn in view of the amendment to the claims. A new rejection is set forth below. Applicant's argument is moot in view of the new rejection necessitated

by the amendment.

32. (**New rejection-necessitated by the amendment**) Claims 1, 3, 5, 6, 7, 9, 14, 22, 24 and 25 are rejected under 35 USC 103(a) as being unpatentable over Kuroda (WO 01/64930, which is PCT/JP01/00926, International publication date: September 7, 2001, cited in IDS. The **US2003/0092069**, which is the National stage of PCT/JP01/00926, is cited as the English translation of WO 01/64930) and Ojala K, *et al*. (Biochem Biophys Res Commun. 2001;284(3):777-84, cited in previous office action).

33. Kuroda (WO 01/64930) teaches hollow nanoparticles composed of HBsAg L protein a biorecognition molecule to introduce a substance (gene, protein, compound, etc.) into the target cells or tissue, wherein the biorecognition molecule on the hollow nanoparticles is an antibody; see the English translation of Abstract (WO 01/64930), and see also see Para [0009]-[0016] and the claims of **US2003/0092069**. Kuroda (WO 01/64930) teaches that the gene encoding HBsAg L protein was mutated in the region of the human liver cell-recognition site (the 3rd to 77th amino acids of the preS region), by introduction of restriction site NotI in the gene); see [0069]-[0072] and Example C of US2003/0092069. This teaching indicates that the HBsAg L protein particle "is modified to lack some of amino acids in a pre-S region" (Claim 9).

Kuroda (WO 01/64930) does not explicitly teach that the antibody is "a cancer specific antibody or anti-virus protein antibody" (e.g. Claim 1), nor "the antibody is displayed on a particle surface by binding to a ZZ tag fused with the particle-forming protein" (e.g. Claim 3)

34. Ojala teaches use of baculovirus (nanoparticle) displaying either a functional

single chain antibody fragment (scFv) specific for the carcinoembryonic antigen (CEA) or the synthetic ZZ tag (IgG binding domains (ZZ) derived from protein A of *Staphylococcus aureus*), see e.g. Abstract. The anti-CEA scFv displaying baculovirus was shown to bind specifically to CEA expressing cells (PC-3). Similarly, the virus displaying the ZZ domains of protein A was targeted to BHK cells *via* binding of an appropriate IgG antibody. In addition, the baculovirus vectors were engineered to incorporate a reporter gene encoding the enhanced green fluorescent protein (EGFP). In all cases, the reporter gene was expressed in the transduced mammalian cells as shown by fluorescence microscopy and flow cytometric analyses. Ojala teaches that such viral particles displaying specific ligand binding moieties have raised an increasing interest in the area of targeted gene therapy, see e.g. Abstract.

35. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the HBsAg L protein nanoparticle of Kuroda by incorporating single chain antibody fragment (scFv) specific for the carcinoembryonic antigen (CEA) or the synthetic ZZ tag in order to target specific cells as taught by Ojala. The skilled artisan would have been motivated to do so, and would have a reasonable expectation of success, given the knowledge that HBsAg L protein comprising Ab can be used as a drug delivery system for delivering a nucleic acid drug, as taught by Kuroda and also given the knowledge that the antibody specific for the carcinoembryonic antigen (CEA) or the synthetic ZZ tag can be used to target specific cells, as taught by Ojala. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

36. (**New rejection-necessitated by the amendment**) Claim 15 is rejected under 35 USC 103(a) as being unpatentable over Kuroda (WO 01/64930) and Ojala , as applied to Claim 1 and 14 above, and further in view of Rosenfeld.

37. Claim 15 is directed to the nanoparticle of Claim 14, wherein the gene comprises HSV-1 *tk* gene.

38. The relevance of Kuroda and Ojala is set forth *supra*. However, O'Riordan does not explicitly teach that HBsAg large particle containing HSV-1 *tk* gene.

39. Rosenfeld teaches an adenoviral particle comprising HSV1 tk gene (AdCMVHSV-1tk) (pp. 610 and 611). Rosenfeld shows that Ad/HSV-1tk particles are highly transducible to human pancreatic carcinoma cells and the resulting carcinoma cells expressing HSV-1 tk protein are more sensitive to chemotherapeutic agent ganciclovir (GCV) (p. 611). Rosenfeld teaches that *in vivo* administration of AdCMVHSV-1tk and GCV results in reduced tumor burden (p. 614 and 615). Rosenfeld suggests a strategy for human pancreatic carcinoma using HSV-tk and GCV in molecular chemotherapy (Abstract).

40. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the nanoparticle of Kuroda to express HSV-1 *tk* as taught by Rosenfeld. The skilled artisan would have been motivated to do so, and would have a reasonable expectation of success, given the knowledge that a nanoparticle comprising HBsAg L protein can be used as a drug delivery system for delivering a nucleic acid drug, as taught by Kuroda, given the knowledge that the antibody specific for the carcinoembryonic antigen (CEA) or the synthetic ZZ tag can target specific cancer cells, as taught by Ojala, and also given the knowledge that the HSV-1 tk substance transferred

into a cell can be used for treatment of a cancer, as taught by Rosenfeld. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

41. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

42. (**Prior rejection-moot**) The rejection of Claims 1-3, 5-7, 22, 24 and 25 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-11 of 10/594, 612 ('612), is moot because '612 has been abandoned.

43. (**Prior rejection-maintained**) The rejection of Claims 1-3, 5-9, 14-16, 22, 24 and 25 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-3, 6, 8 and 9 of co-pending application **11/987,476, is**

maintained. Applicant acknowledges the rejection and does not wish to prematurely respond.

Remarks

44. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business

Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648